

Claims

- 5 1. Use of an agonist of an hypothalamic hormone for the preparation of a pharmaceutical agent for the infertility treatment of female mammals, wherein the agonist is a GnRH agonist and the pharmaceutical agent is suitable to be used for luteal phase support.
- 10 2. Use according to claim 1, wherein the pharmaceutical agent is suitable to be used for luteal phase support after a spontaneous ovulation.
- 15 3. Use according to claim 1, wherein the pharmaceutical agent is suitable to be used for luteal phase support after stimulation of follicular growth and induction of final follicular maturation and ovulation with one or more additional agents.
- 20 4. Use according to claim 3, wherein the additional agent triggering final follicular maturation and ovulation is a GnRH agonist.
- 25 5. Use according to claim 3 and 4, wherein the additional agent triggering final follicular maturation and ovulation is the GnRH agonist used to support the luteal phase.
6. Use according to claim 3 and 4, wherein additional agent triggering final follicular maturation and ovulation is a GnRH agonist different from the GnRH agonist used to support the luteal phase.
- 25 7. Use according to claims 2 to 3, wherein the pharmaceutical agent suitable for luteal phase support is used after administration of a GnRH antagonist during the last days of follicular growth stimulation.

8. Use according to any of the preceding claims, wherein the pharmaceutical agent suitable for luteal phase support is administered in combination with natural progesterone, a progestagen, hCG, LH, one or more isoform of LH or of hCG, a peptidomimetic of LH or of hCG, an LH or an hCG analog with a modified pharmacokinetic, a phosphodiesterase inhibitor, a non-peptidic modulator of cyclicAMP or a combination of two or more of these agents.
9. Use according to claim 1 to 7, wherein the pharmaceutical agent suitable for luteal phase support is administered in combination with a cytokine involved in the embryo implantation mechanisms.
10. Use according to claim 9, wherein the cytokine is native LIF, recombinant LIF, a peptide or a non-peptide agonist analog of LIF.
11. Use according to claim 1 to 10, wherein the stimulation with an additional agent is followed, before ovulation, by an oocyte retrieval procedure.
12. Use according to claim 11, wherein oocytes are to undergo an *in vitro* maturation.
13. Use according to claim 11, wherein oocytes are to undergo an *in vitro* fertilization.
14. Use according to claims 1 to 10, wherein the stimulation with an additional agent is followed, after ovulation trigger, with an insemination (IUI).
15. Use according to any of the preceding claims, wherein the GnRH agonist route of administration is intra-nasal, oral, sub-cutaneous, intra-muscular, vaginal, rectal, transdermal, or pulmonary.
16. Use according to any of the proceeding claims, wherein the GnRH agonist is a natural (native) GnRH, a recombinant GnRH, a synthetic peptide agonist of GnRH, a non-peptidic GnRH agonist, or a molecular chimera of GnRH.

17. Use according to claim 16, wherein the GnRH agonist is selected from the group comprising buserelin(e), nafarelin(e), triptorelin(e), leuprorelin(e), goserelin(e), deslorelin(e) and histrelin(e), analogs thereof or a combination of two or more of these
5 agonists.

18. Use according to claim 3, wherein the additional agent stimulating follicular growth is selected from the group comprising hMG, urine-derived FSH, recombinant FSH, one or several FSH isoforms, FSH mimetics, FSH analogs with a modified
10 pharmacokinetic, SERM, aromatases inhibitors, phosphodiesterase inhibitors, or a combination of two or more of these agents.

19. Use according to claim 18, wherein SERM are selected from the group comprising clomiphen(e), tamoxifen(e), or raloxifen(e) or a combination of two or more of these
15 agents.

20. Use according to claim 18, wherein the aromatase inhibitor is selected from the group comprising anastrozol, letrozol or exemestane or a combination of two or more of these agents.

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21. Use according to claim 3, wherein the additional agent triggering final follicular maturation and ovulation is selected from the group comprising hCG, LH, one or more isoforms of hCG or LH, hCG and LH peptido-mimetics, hCG and LH analogs with a modified pharmacokinetic, phosphodiesterase inhibitors or a combination of two or more
25 of these agents.

22. Use according to claim 18 or 21, wherein the phosphodiesterase inhibitor is theophylline.

30 23. Use according to any of the preceding claims, wherein the female mammal is a woman.

24. Use according to claim 17, wherein the GnRH agonist is buserelin.

25. Use according to claim 24, wherein buserelin administration is started within the first three days following ovulation trigger.

5 26. Use according to claim 25, wherein buserelin administration is started on the first day following ovulation trigger.

27. Use according to claim 24, 25, and 26 wherein buserelin is administered intra-nasally at a dose between 50 and 400 µg.

10 28. Use according to claim 27, wherein buserelin is administered intra-nasally at a dose of 100 µg.

29. Use according to claim 28, wherein buserelin is administered at a frequency

15 between three times a day and once every three days.

30. Use according to claim 29, wherein buserelin is administered at a frequency of one administration every day.

20 31. Use according to claim 29, wherein buserelin is administered during 7 to 28 days.

32. Use according to claim 29, wherein buserelin is administered during 14 days.

25 33. Use according to claim 4, 5 et 6, wherein the GnRH agonist is buserelin and is administered intra-nasally, once at a dose between 50 and 600 µg.

34. Use according to claim 33 wherein buserelin is administered intra-nasally at a dose of 200 µg.

30 35. Use according to claim 1, wherein the pharmaceutical agent is embedded in a biocompatible polymer matrix allowing sustained and controlled release.

36. Patient Kit for the treatment of infertility in female mammals which includes:

- a GnRH agonist according to claim 1,
- one or more additional agents to trigger final follicular maturation, and ovulation according to claims 4, 5, 6, 17 et 21.

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37. Patient Kit according to claim 36, wherein the pharmaceutical agent is the GnRH agonist used for the luteal support and wherein the GnRH agonist is formulated in dosage and unit required for one cycle of treatment.

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38. Method of treatment for female mammals infertility, using a pharmaceutical agent which includes a GnRH agonist suitable for luteal phase support.

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39. Method according to claim 38, wherein the pharmaceutical agent is suitable for use as luteal support after a spontaneous ovulation.

40. Method according to claim 38, wherein the pharmaceutical agent is suitable to be used for luteal phase support after stimulation of follicular growth and induction of final follicular maturation and ovulation with one or more additional agents.

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41. Method according to claim 40, wherein the additional agent triggering final follicular maturation and ovulation is a GnRH agonist.

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42. Method according to claims 40 and 41, wherein the additional agent triggering final follicular maturation and ovulation is the GnRH agonist used to support the luteal phase.

43. Method according to claims 40 and 41, wherein additional agent triggering final follicular maturation and ovulation is a GnRH agonist different from the GnRH agonist used to support the luteal phase.

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44. Method according to claim 39 nad 40, wherein the pharmaceutical agent suitable for luteal support is used after administration of a GnRH antagonist during the last days of follicular growth stimulation.

45. Method according to claim 38 to 44, wherein the pharmaceutical agent suitable for luteal phase support is administered in combination with natural progesterone, a progestagen, hCG, LH, one or more isoform of LH or of hCG, a peptidomimetic of LH or 5 of hCG, an LH or an hCG analog with a modified pharmacokinetic, a phosphodiesterase inhibitor, a non-peptidic modulator of cyclicAMP or a combination of two or more of these agents.

46. Method according to claim 38 to 44, wherein the pharmaceutical agent suitable for 10 luteal phase support is administered in combination with a cytokine involved in the embryo implantation mechanisms.

47. Method according to claim 46, wherein the cytokine is native LIF, recombinant LIF, a peptidic or a non-peptidic agonist analog of LIF. 15

48. Method according to claim 38 to 47, wherein the stimulation with an additional agent is followed, before ovulation, by an oocyte retrieval procedure.

49. Method according to claim 48, wherein oocytes are to undergo an *in vitro* 20 maturation.

50. Method according to claim 48, wherein oocytes are to undergo an *in vitro* fertilization.

25 51. Method according to claims 38 to 47, wherein the stimulation with an additional agent is followed, after ovulation trigger, with an insemination (IUI).

52. Method according to claims 39 to 51, wherein the GnRH agonist route of 30 administration is intra-nasal, oral, sub-cutaneous, intra-muscular, vaginal, rectal, transdermal, or pulmonary.

53. Method according to claims 39 to 52, wherein the GnRH agonist is a natural (native) GnRH, a recombinant GnRH, a synthetic peptide agonist of GnRH, a non-peptide GnRH agonist, or a molecular chimera of GnRH.

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54. Method according to claim 53, wherein the GnRH agonist is selected from the group comprising buserelin(e), nafarelin(e), triptorelin(e), leuprorelin(e), goserelin(e), deslorelin(e) and histrelin(e), analogs thereof or a combination of two or more of these agonists.

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55. Method according to claim 41, wherein the additional agent stimulating follicular growth is selected from the group comprising hMG, urine-derived FSH, recombinant FSH, one or several FSH isoforms, FSH mimetics, FSH analogs with a modified pharmacokinetic, SERM, aromatases inhibitors, phosphodiesterase inhibitors, or a combination of two or more of these agents.

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56. Method according to claim 55, wherein SERM are selected from the group comprising clomiphene(e), tamoxifen(e), or raloxifen(e) or a combination of two or more of these agents.

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57. Method according to claim 55, wherein the aromatase inhibitor is selected from the group comprising anastrozole, letrozole or exemestane or a combination of two or more of these agents.

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58. Method according to claim 41, wherein the additional agent triggering final follicular maturation and ovulation is selected from the group comprising hCG, LH, one or more isoforms of hCG or LH, hCG and LH peptido-mimetics, hCG and LH analogs with a modified pharmacokinetic, phosphodiesterase inhibitors or a combination of two or more of these agents.

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59. Method according to claims 55 and 58, wherein the phosphodiesterase inhibitor is theophylline.

60. Method according to claim 37, wherein the female mammal is a woman.

61. Method according to claim 54, wherein the GnRH agonist is buserelin.

5 62. Method according to claim 61, wherein buserelin administration is started within the first three days following ovulation trigger.

63. Method according to claim 62, wherein buserelin administration is started on the
10 first day following ovulation trigger.

64. Method according to claims 61, 62 and 63, wherein buserelin is used intra-nasally at a dose between 50 and 400 µg.

15 65. Method according to claim 64, wherein buserelin is used intra-nasally at a dose of 100 µg.

66. Method according to claims 61, 62 and 63, wherein buserelin is used at a frequency between three times a day and once every three days.

20 67. Method according to claim 66, wherein buserelin is used at a frequency of one administration every day.

68. Method according to claim 61, 62 and 63, wherein buserelin is administered during
25 7 to 28 days.

69. Method according to claim 68, wherein buserelin is administered during 14 days.

70. Method according to claim 42, wherein the GnRH agonist is buserelin and is
30 administered intra-nasally, once, at a dose between 50 and 600 µg.

71. Method according to claim 70, wherein buserelin is administered intra-nasally at a dose of 200 µg.

72. Method according to claim 39, wherein the pharmaceutical agent is embedded in a biocompatible polymer matrix allowing sustained and controlled release.